

FILE 'EMBASE' ENTERED AT 13:03:05 ON 02 MAY 2005  
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FILE 'BIOSIS' ENTERED AT 13:03:05 ON 02 MAY 2005  
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FILE 'SCISEARCH' ENTERED AT 13:03:05 ON 02 MAY 2005  
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FILE 'MEDLINE' ENTERED AT 13:03:05 ON 02 MAY 2005

=> s mmp (w) 12 or (macrophage elastase) or metalloelastase  
L2 1380 MMP (W) 12 OR (MACROPHAGE ELASTASE) OR METALLOELASTASE

=> s antisense or oligonucleotide  
L3 252733 ANTISENSE OR OLIGONUCLEOTIDE

=> s 12 and 13  
L4 27 L2 AND L3

=> dup rem 14  
PROCESSING COMPLETED FOR L4  
L5 17 DUP REM L4 (10 DUPLICATES REMOVED)

=> d 1-17 15 iall

L5 ANSWER 1 OF 17 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 1

ACCESSION NUMBER: 2004330402 EMBASE

TITLE: Colony-stimulating factor-1 blockade by **antisense oligonucleotides** and small interfering RNAs suppresses growth of human mammary tumor xenografts in mice.

AUTHOR: Aharinejad S.; Paulus P.; Sioud M.; Hofmann M.; Zins K.; Schafer R.; Stanley E.R.; Abraham D.

CORPORATE SOURCE: S. Aharinejad, Lab. for Cardiovascular Research, Dept. of Anatomy and Cell Biology, Vienna Medical University, Waehringerstrasse 13, A-1090 Vienna, Austria.  
seyedhossein.aharinejad@meduniwien.ac.at

SOURCE: Cancer Research, (1 Aug 2004) Vol. 64, No. 15, pp. 5378-5384.

Refs: 47

ISSN: 0008-5472 CODEN: CNREA8

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 016 Cancer

022 Human Genetics

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20040826

Last Updated on STN: 20040826

ABSTRACT: Colony-stimulating factor (CSF)-1 is the primary regulator of tissue macrophage production. CSF-1 expression is correlated with poor prognosis in breast cancer and is believed to enhance mammary tumor progression and metastasis through the recruitment and regulation of tumor-associated macrophages. Macrophages produce matrix metalloproteases (MMPs) and vascular endothelial growth factor, which are crucial for tumor invasion and angiogenesis. Given the important role of CSF-1, we hypothesized that blockade of CSF-1 or the CSF-1 receptor (the product of the c-fms proto-oncogene) would suppress macrophage infiltration and mammary tumor growth. Human MCF-7 mammary carcinoma cell xenografts in mice were treated with either mouse CSF-1 \*\*\*antisense\*\*\* **oligonucleotide** for 2 weeks or five intratumoral

injections of either CSF-1 small interfering RNAs or c-fms small interfering RNAs. These treatments suppressed mammary tumor growth by 50%, 45%, and 40%, respectively, and selectively down-regulated target protein expression in tumor lysates. Host macrophage infiltration; host **MMP-12**, MMP-2, and vascular endothelial growth factor A expression; and endothelial cell proliferation within tumors of treated mice were decreased compared with tumors in control mice. In addition, mouse survival significantly increased after CSF-1 blockade. These studies demonstrate that CSF-1 and CSF-1 receptor are potential therapeutic targets for the treatment of mammary cancer.

CONTROLLED TERM: Medical Descriptors:  
\*breast tumor: ET, etiology  
\*tumor xenograft  
\*cancer inhibition  
macrophage  
prognosis  
tumor growth  
metastasis  
tumor associated leukocyte  
receptor blocking  
cancer invasion: ET, etiology  
tumor vascularization: ET, etiology  
angiogenesis  
tumor angiogenesis  
proto oncogene  
proto oncogene c fms  
cell infiltration  
macrophage infiltration  
protein expression  
cell lysate  
tumor lysate  
endothelium cell  
cell proliferation  
survival  
human  
nonhuman  
female  
mouse  
animal model  
controlled study  
human cell  
animal tissue  
animal cell  
adolescent  
article  
priority journal  
Drug Descriptors:  
\*colony stimulating factor 1  
\***antisense oligodeoxynucleotide**  
\*small interfering RNA  
colony stimulating factor receptor  
colony stimulating factor 1 receptor  
matrix metalloproteinase  
vasculotropin  
gene product  
\***macrophage elastase**  
gelatinase A  
vasculotropin A  
unclassified drug  
CAS REGISTRY NO.: (colony stimulating factor 1) 81627-83-0; (vasculotropin)  
127464-60-2; (gelatinase A) 146480-35-5; (vasculotropin A)  
489395-96-2

L5 ANSWER 2 OF 17

MEDLINE on STN

ACCESSION NUMBER: 2004402386 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15307189

TITLE: Reduced intragraft mRNA expression of matrix metalloproteinases Mmp3, Mmp12, Mmp13 and Adam8, and diminished transplant arteriosclerosis in Ccr5-deficient mice.

AUTHOR: Luckow Bruno; Joergensen Joanne; Chilla Silvia; Li Jian-Ping; Henger Anna; Kiss Eva; Wieczorek Grazyna; Roth Lukas; Hartmann Nicole; Hoffmann Reinhard; Kretzler Matthias; Nelson Peter J; Perez de Lema Guillermo; Maier Holger; Wurst Wolfgang; Balling Rudi; Pfeffer Klaus; Grone Hermann-Josef; Schlondorff Detlef; Zerwes Hans-Gunter

CORPORATE SOURCE: Klinikum der Universitat Munchen, Medizinische Poliklinik--Innenstadt, Munchen, Germany..  
bruno.luckow@med.uni-muenchen.de

SOURCE: European journal of immunology, (2004 Sep) 34 (9) 2568-78.  
Journal code: 1273201. ISSN: 0014-2980.

PUB. COUNTRY: Germany: Germany, Federal Republic of

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200410

ENTRY DATE: Entered STN: 20040813

Last Updated on STN: 20041008

Entered Medline: 20041007

#### ABSTRACT:

Experimental and human organ transplant studies suggest an important role for chemokine (C-C-motif) receptor-5 (CCR5) in the development of acute and chronic allograft rejection. Because early transplant damage can predispose allografts to chronic dysfunction, we sought to identify potential pathophysiologic mechanisms leading to allograft damage by using wild-type and Ccr5-deficient mice as recipients of fully MHC-mismatched heart and carotid-artery allografts. Gene expression in rejecting heart allografts was analyzed 2 and 6 days after transplantation using Affymetrix GeneChips. Microarray analysis led to identification of four metalloproteinase genes [matrix metalloproteinase (Mmp)3, Mmp12, Mmp13 and a disintegrin and metalloprotease domain (Adam)8] with significantly diminished intragraft mRNA expression in Ccr5-deficient mice at day 6. Accordingly, allografts from Ccr5-deficient mice showed less tissue remodeling and hence better preservation of the myocardial architecture compared with allografts from wild-type recipients. Moreover, survival of cardiac allografts was significantly increased in Ccr5-deficient mice. Carotid artery allografts from Ccr5-deficient recipients showed better tissue preservation, and significant reduction of neointima formation and CD3+ T cell infiltration. Ccr5 appears to play an important role in transplant-associated arteriosclerosis that may involve metalloproteinase-mediated vessel wall remodeling. We conclude that early tissue remodeling may be a critical feature in the predisposition of allografts to the development of chronic dysfunction. Copyright 2004 Wiley-VCH Verlag GmbH & Co.

#### CONTROLLED TERM:

Animals

\*Antigens, CD: GE, genetics

\*Arteriosclerosis: PC, prevention & control

Carotid Arteries: TR, transplantation

\*Collagenases: GE, genetics

Cyclosporine: PD, pharmacology

\*Heart Transplantation: AE, adverse effects

\*Membrane Proteins: GE, genetics

\*Metalloendopeptidases: GE, genetics

Mice

Mice, Inbred BALB C

Mice, Inbred C57BL

\*Oligonucleotide Array Sequence Analysis

\*RNA, Messenger: AN, analysis

\*Receptors, CCR5: PH, physiology  
Research Support, Non-U.S. Gov't  
\*Stromelysin 1: GE, genetics  
Transplantation, Homologous  
CAS REGISTRY NO.: 59865-13-3 (Cyclosporine)  
CHEMICAL NAME: 0 (Antigens, CD); 0 (Membrane Proteins); 0 (RNA, Messenger); 0 (Receptors, CCR5); EC 3.4.24 (Metalloendopeptidases); EC 3.4.24.- (Adam8 protein, mouse); EC 3.4.24.- (Collagenases); EC 3.4.24.- (alveolar macrophage elastase); EC 3.4.24.- (collagenase 3); EC 3.4.24.17 (Stromelysin 1)

L5 ANSWER 3 OF 17 MEDLINE on STN  
ACCESSION NUMBER: 2004037774 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 14647437  
TITLE: MMP expression profiling in recurrent stage IB lung cancer.  
AUTHOR: Cho Nam Hoon; Hong Kyi Pyo; Hong Sung Hui; Kang Suki; Chung Kyung Young; Cho Sang Ho  
CORPORATE SOURCE: Department of Pathology, Yonsei University College of Medicine, Seoul, Korea.  
SOURCE: Oncogene, (2004 Jan 22) 23 (3) 845-51.  
Journal code: 8711562. ISSN: 0950-9232.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: . Priority Journals  
ENTRY MONTH: 200403  
ENTRY DATE: Entered STN: 20040123  
Last Updated on STN: 20040304  
Entered Medline: 20040303

ABSTRACT:

We aimed to clarify the prime role of recurrence in stage I lung cancer. To determine the expression profiles, quantitative RT-PCR and real-time PCR were performed subsequently to evaluate the validity of meaningful molecules identified by 0.12 K c-DNA array experiment surveys. In all, 10 lung cancer patients presenting with recurrence of stage IB were selected and compared with 10 stage IB lung cancer patients without recurrence since biopsied 3 years previously. On c-DNA microarray data analysis using pairs of recurred and the corresponding nonrecurred patients, the following genes were found to be upregulated in the recurred cases: matrix metalloproteinase (MMP)-10 in five cases, **MMP-12** in two cases, MMP-11, MMP-14, MMP-15, fos, cyclin E2, E2F3, TGF-alpha in each one case. The most frequently upregulated genes in recurred lung cancers were MMP-10 (stromelysin-2) and **MMP-\*\*\*12\*\*\* (macrophage elastase)**. On transcriptional assay by quantitative RT-PCR and real-time RT-PCR analysis to validate those molecules, both transcripts of MMP-10 and **MMP-12** were significantly more upregulated in recurrent stage IB lung cancer than in the non-recurred stage IB lung cancer (P=0.004). Transcript levels were identical to c-DNA array data. The protein levels of these entities were also evaluated by immunohistochemistry of archival slides. By immunohistochemistry, MMP-10 monoclonal antibody showed more intense immunoreactivity in the recurred stage IB lung cancer than in the nonrecurred stage IB lung cancer (P=0.0313). Our approach revealed that MMP-10 plays an important role in the recurrence in stage IB lung cancer, irrespective of the histologic type.

CONTROLLED TERM: Base Sequence  
Carcinoma, Non-Small-Cell Lung: EN, enzymology  
\*Carcinoma, Non-Small-Cell Lung: GE, genetics  
DNA Primers  
\*Gene Expression Profiling  
Humans  
Immunohistochemistry  
Lung Neoplasms: EN, enzymology  
\*Lung Neoplasms: GE, genetics

\*Matrix Metalloproteinases: GE, genetics  
**Oligonucleotide Array Sequence Analysis**  
Recurrence

Research Support, Non-U.S. Gov't  
Reverse Transcriptase Polymerase Chain Reaction  
Transcription, Genetic

CHEMICAL NAME: 0 (DNA Primers); EC 3.4.24.- (Matrix Metalloproteinases)

L5 ANSWER 4 OF 17 MEDLINE on STN

ACCESSION NUMBER: 2004113115 MEDLINE

DOCUMENT NUMBER: PubMed ID: 14644759

TITLE: Lysosomal acid lipase deficiency causes respiratory  
inflammation and destruction in the lung.

AUTHOR: Lian Xuemei; Yan Cong; Yang Li; Xu Yan; Du Hong

CORPORATE SOURCE: Div. of Human Genetics, Cincinnati Children's Hospital  
Medical Center, 3333 Burnet Ave., Cincinnati, OH  
45229-3039, USA.

CONTRACT NUMBER: DK-54930 (NIDDK)

HL-061803 (NHLBI)

HL-067862 (NHLBI)

SOURCE: American journal of physiology. Lung cellular and molecular  
physiology, (2004 Apr) 286 (4) L801-7. Electronic  
Publication: 2003-11-26.

Journal code: 100901229. ISSN: 1040-0605.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200404

ENTRY DATE: Entered STN: 20040309

Last Updated on STN: 20040427

Entered Medline: 20040426

**ABSTRACT:**

The functional roles of neutral lipids are poorly understood in the lung. Blocking cholesteryl ester and triglyceride metabolism in lysosomal acid lipase gene knockout mice (lal-/-) resulted in a high level of neutrophil influx in the lungs as early as 2 mo of age. Bronchoalveolar macrophages appeared foamy and gradually increased in number with age progression. Affymetrix GeneChip array analysis of lung mRNA showed increased levels of proinflammatory cytokine (including IL-1beta, IL-6, and TNF-alpha) and matrix metalloproteinase (including MMP-8, MMP-9, and **MMP-12**) expression in lal-/- mice. With age progression, some areas of lal-/- mice developed severe abnormal cell proliferation and alveolar remodeling. In other areas, alveolar destruction (i.e., emphysema) was observed. In addition, Clara cell hypertrophy and hyperplasia developed in conducting airways. The pathophysiological phenotypes in the lal-/- mouse lungs became more severe with increasing age. The studies support the concept that neutral lipid metabolites play essential roles in pulmonary homeostasis, inflammatory responses, remodeling, and injury repair.

**CONTROLLED TERM:**

Animals

Chemokines: GE, genetics

Cytokines: GE, genetics

Emphysema: IM, immunology

\*Emphysema: ME, metabolism

\*Emphysema: PA, pathology

Hyperplasia

Hypertrophy

Lipase: DF, deficiency

\*Lipase: GE, genetics

Lipids: ME, metabolism

Lysosomes: EN, enzymology

Macrophages, Alveolar: IM, immunology

Matrix Metalloproteinases: GE, genetics

Mice  
Mice, Mutant Strains  
Neutrophils: IM, immunology  
**Oligonucleotide Array Sequence Analysis**

Phenotype

Pneumonia: IM, immunology  
\*Pneumonia: ME, metabolism  
\*Pneumonia: PA, pathology  
Pulmonary Alveoli: IM, immunology  
Pulmonary Alveoli: ME, metabolism  
Pulmonary Alveoli: PA, pathology  
Research Support, Non-U.S. Gov't  
Research Support, U.S. Gov't, P.H.S.

CHEMICAL NAME: 0 (Chemokines); 0 (Cytokines); 0 (Lipids); EC 3.1.1.3 (Lipase); EC 3.4.24.- (Matrix Metalloproteinases)

L5 ANSWER 5 OF 17 MEDLINE on STN

ACCESSION NUMBER: 2003113667 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12626598

TITLE: Macrophage **metalloelastase** as a major factor for glomerular injury in anti-glomerular basement membrane nephritis.

AUTHOR: Kaneko Yoshikatsu; Sakatsume Minoru; Xie Yuansheng; Kuroda Takeshi; Igashima Michiko; Narita Ichiei; Gejyo Fumitake  
CORPORATE SOURCE: Division of Clinical Nephrology and Rheumatology, Niigata University Graduate School of Medical and Dental Sciences and Kidney Center, Shinraku-en Hospital, Niigata, Japan.. kanekoy@med.niigata-u.ac.jp

SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2003 Mar 15) 170 (6) 3377-85.

Journal code: 2985117R. ISSN: 0022-1767.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200306

ENTRY DATE: Entered STN: 20030311

Last Updated on STN: 20030626

Entered Medline: 20030625

ABSTRACT:

Rat anti-glomerular basement membrane (GBM) nephritis is a model of crescentic glomerulonephritis induced by injection of anti-GBM antiserum. To elucidate the mechanism of glomerular injury, we analyzed the gene expression patterns in the kidneys of anti-GBM nephritis rats using DNA arrays, and found that macrophage **metalloelastase**/matrix metalloproteinase (**MMP**)-

\*\*\*12\*\*\* was one of the highly expressed genes in the kidneys on days 3 and 7 after the injection of anti-GBM antiserum. Enhancement of **MMP**-

\*\*\*12\*\*\* mRNA expression was confirmed by Northern blot analysis, and in situ hybridization revealed that **MMP-12** mRNA was expressed in

ED-1-positive macrophages and multinuclear giant cells in the glomeruli with crescent. Moreover, these cells were positive with anti-rat rMMP-12 Ab on the section of the kidneys of anti-GBM nephritis rats on day 7. To clarify the role of **MMP-12**, we conducted a neutralization experiment

using anti-rat rMMP-12 Ab, which had an ability to inhibit rMMP-12 activity of degrading natural substrate such as bovine elastin or human fibronectin in vitro. Anti-rat rMMP-12 Ab or control Ig was injected in each of six rats on days 0, 2, 4, and 6 after the injection of anti-GBM antiserum. Consequently, crescent formation and macrophage infiltration in the glomeruli were significantly reduced in the rats treated with anti-rat rMMP-12 Ab, and the amount of urine protein was also decreased. These results disclosed that

\*\*\*MMP\*\*\* -12 played an important role in glomerular injury in a crescentic glomerulonephritis model, and inhibition of **MMP-12** may lead to a new therapeutic strategy for this disease.

CONTROLLED TERM: Check Tags: Male  
 Animals  
 \*Anti-Glomerular Basement Membrane Disease: EN, enzymology  
 Anti-Glomerular Basement Membrane Disease: IM, immunology  
 \*Anti-Glomerular Basement Membrane Disease: PA, pathology  
 Anti-Glomerular Basement Membrane Disease: PC, prevention  
 & control  
 Blotting, Northern  
 Blotting, Western  
 Cell Movement: IM, immunology  
 Gene Expression Regulation: IM, immunology  
 Immune Sera: AD, administration & dosage  
 In Situ Hybridization  
 Injections, Intravenous  
 \*Kidney Glomerulus: EN, enzymology  
 \*Kidney Glomerulus: PA, pathology  
 \*Macrophages: EN, enzymology  
 \*Metalloendopeptidases: AE, adverse effects  
 Metalloendopeptidases: BI, biosynthesis  
 Metalloendopeptidases: GE, genetics  
**Oligonucleotide Array Sequence Analysis**  
 Rats  
 Rats, Inbred WKY  
 Recombinant Proteins: AD, administration & dosage  
 Recombinant Proteins: TU, therapeutic use  
 Research Support, Non-U.S. Gov't  
 Substrate Specificity

CHEMICAL NAME: 0 (Immune Sera); 0 (Recombinant Proteins); EC 3.4.24  
 (Metalloendopeptidases); EC 3.4.24.- (alveolar  
**macrophage elastase)**

L5 ANSWER 6 OF 17 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on  
 STN

ACCESSION NUMBER: 2003:900605 SCISEARCH

THE GENUINE ARTICLE: 732KR

TITLE: Comparing genomic and histologic correlations to  
 radiographic changes in tumors: A murine SCCVII model  
 study

AUTHOR: Yang Y S; Guccione S; Bednarski M D (Reprint)

CORPORATE SOURCE: Stanford Univ, Sch Med, Dept Radiol, MRS Res Ctr,  
 Stanford, CA 94305 USA (Reprint); NIH, Ctr Clin, Radiol &  
 Imaging Sci Program, Bethesda, MD 20892 USA

COUNTRY OF AUTHOR: USA

SOURCE: ACADEMIC RADIOLOGY, (OCT 2003) Vol. 10, No. 10, pp. ✓  
 1165-1175.  
 Publisher: ASSOC UNIV RADIOLOGISTS, 820 JORIE BLVD, OAK  
 BROOK, IL 60523-2251 USA.  
 ISSN: 1076-6332.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 54

ABSTRACT:

Rationale and Objectives. To investigate the correlation between the  
 temporal changes in T1- and T2-weighted contrast-enhanced magnetic resonance  
 imaging (MRI), histologic evaluation, and genomic analysis using  
 \*\*\*oligonucleotide\*\*\* microarrays in a murine squamous cell carcinoma tumor  
 models.

Materials and Methods. The squamous cell carcinoma (SCC VII) cell line was  
 used to initiate subcutaneous tumors in mice. This mouse model has been used as  
 a model for human head and neck carcinomas. Animals were imaged using contrast  
 enhanced MRI (CE-MRI). Different stages of tumor growth were defined based on  
 changes in the T1- and T2-weighted MRI patterns. The contrast enhancing (CE)  
 and nonenhancing (NE) regions of the tumors were marked and biopsied for

\*\*\*oligonucleotide\*\*\* microarray and histologic analysis. Tumors with no differential contrast enhancement were used as controls.

Results. Distinct temporal stages of tumor progression can be defined using both T1- and T2-weighted CE-MRI and microarray analysis. The early stage tumors show a homogeneous contrast enhancement pattern in the T1- and T2-weighted images with no significant differential gene expression from the center and periphery of the tumor. The more advanced tumors that show discrete regions of contrast enhancement in the post-contrast T1-weighted MRIs and tissues from the CE and NE regions show distinctly differential gene expression profiles. Histologic analysis (hematoxylin-eosin stain) showed that the samples obtained from the periphery and center of the early stage tumors and the CE and NE regions from these more advanced tumors were similar. The gene expression profiles of late-stage tumors that showed changes in T2-weighted MRI signal intensity were consistent with tissue degradation in the NE region, which also showed characteristic signs of tissue necrosis in histologic analysis.

Conclusion. These results show that temporal changes in T1- and T2-weighted CE-MRI are related to distinct gene expression profiles, and histologic analysis may not be sufficient to detect these detailed changes. As tumors progress, discrete regions of post-contrast T1 enhancement are identified; these regions have distinct gene expression patterns despite similar histologic features. In late-stage tumors, regions of T2 signal changes are observed which correspond with tissue necrosis.

CATEGORY: RADIOLOGY, NUCLEAR MEDICINE & MEDICAL IMAGING  
 SUPPLEMENTARY TERM: contrast-enhanced magnetic resonance imaging (MRI); functional genomics; microarray analysis; animal tumor model; histologic analysis  
 SUPPL. TERM PLUS: ENDOTHELIAL GROWTH-FACTOR; SQUAMOUS-CELL CARCINOMA; ANGIOGENESIS IN-VITRO; GENE-EXPRESSION; MACROPHAGE METALLOELASTASE; MOLECULAR CLASSIFICATION; EXTRACELLULAR-MATRIX; MAGNETIC-RESONANCE; CANCER; INTERLEUKIN-1

REFERENCE(S):

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
ADAMS A E	1999	24	305	BONE
ALEXANDER J	2003			P 89 ANN M RAD SOC N
ALIZADEH A A	2000	403	503	NATURE
ANDERSON G R	2001	81	501	CURR SCI INDIA
BATTEGAY E J	1994	125	917	J CELL BIOL
BITTNER M	2000	406	536	NATURE
BORK P	1993	327	125	FEBS LETT
BOSTROM P J	2000	88	417	INT J CANCER
BRASCH R	1997	7	68	JMRI-J MAGN RESON IM
CLARK E A	2000	406	532	NATURE
COCHRAN A J	2000	30	11	SEMIN NUCL MED
DENIZOT F	1989	19	631	EUR J IMMUNOL
DIMITRIADOU V	1997	17	1541	ANTICANCER RES
DINARELLO C A	2000	343	732	NEW ENGL J MED
DINARELLO C A	1996	87	2095	BLOOD
FERRARA N	1999	5	1359	NAT MED
GALE N W	1999	13	1055	GENE DEV
GILLIES R J	2000	2	139	NEOPLASIA
GOLUB T R	1999	286	531	SCIENCE
GORRINRIVAS M J	2000	6	1647	CLIN CANCER RES
GORRINRIVAS M J	2000	231	67	ANN SURG
GOURDON G	1995	86	766	BLOOD
GRIMBERG A	2000	183	1	J CELL PHYSIOL
GUCCIONE S	2003	228	560	RADIOLOGY
GUCCIONE S	2002			P 88 ANN M RAD SOC N
GUCCIONE S	2003			P ANN M AM SOC CLIN
HELDIN C H	1999	79	1283	PHYSIOL REV



HOMER J J	2000	25	169	CLIN OTOLARYNGOL
JOHANSSON N	2000	57	5	CELL MOL LIFE SCI
KAO C M	1999	15	304	BIOTECHNOL PROGR
KIM S	2000	252	173	GENE
KIM J E	2000	77	169	J CELL BIOCHEM
MASHIMA T	2001	188	352	J CELL PHYSIOL
MCKINNON P J	2000	20	656	MOL CELL BIOL
MIANO J M	2000	87	355	CIRC RES
MIETTINEN M	1999	22	219	J HISTOTECHNOL
NAKAJIMA M	2002	178	99	CANCER LETT
NEEMAN M	2001	11	70	SEMIN RADIAT ONCOL
NICOSIA R F	1994	145	1023	AM J PATHOL
NING S C	1999	50	215	RADIOTHER ONCOL
PEROU C M	1999	96	9212	P NATL ACAD SCI USA
PEROU C M	2000	406	747	NATURE
PHAM C	1992	16	225	CANC INVEST
PUPA S M	2002	192	259	J CELL PHYSIOL
RICKWELL S	2001		133	TUMOUR MICROENVIRONM
RUOSLAHTI E	1999	76	1	ADV CANCER RES
SCHERF U	2000	24	236	NAT GENET
TAE K	2000	6	2821	CLIN CANCER RES
TRIMBOM T	1998	13	112	GENE DEV
VANDERREST M	1991	5	2814	FASEB J
VOGEL T	1994	18	274	J CELL BIOCHEM
WESTERMARCK J	1999	13	781	FASEB J
WU T D	2001	195	53	J PATHOL
ZIEMER L S	2001	3	500	NEOPLASIA

L5 ANSWER 7 OF 17

MEDLINE on STN

ACCESSION NUMBER: 2003434368 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12963695

TITLE: Matrilysin-dependent elastolysis by human macrophages.

AUTHOR: Filippov Sergey; Caras Ingrid; Murray Richard; Matrisian Lynn M; Chapman Harold A Jr; Shapiro Steven; Weiss Stephen J

CORPORATE SOURCE: University of Michigan Comprehensive Cancer Center, Ann Arbor, MI 48109, USA.

CONTRACT NUMBER: AI21301 (NIAID)

SOURCE: Journal of experimental medicine, (2003 Sep 15) 198 (6) 925-35. Electronic Publication: 2003-09-08. Journal code: 2985109R. ISSN: 0022-1007.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200311

ENTRY DATE: Entered STN: 20030917  
Last Updated on STN: 20031108  
Entered Medline: 20031107

ABSTRACT:

Human macrophages found in juxtaposition to fragmented elastin in vivo express the elastolytic matrix metalloproteinases (MMPs) progelatinase B, prometalloelastase, and promatrilysin. Though MMPs can degrade a range of extracellular matrix components, increasing evidence suggests that preferred targets in vivo include nonmatrix substrates such as chemokines and growth factors. Hence, the means by which MMPs participate in elastin turnover remain undefined as does the identity of the elastolysins. Herein, human macrophage cultures have been established that express a complement of elastolytic proteinases similar, if not identical, to that found in vivo. Under plasminogen-free conditions, macrophages preferentially use \*\*\*metalloelastase\*\*\* to mediate elastolysis via a process that deposits active enzyme on elastin surfaces. By contrast, in the presence of plasminogen, human macrophages up-regulate proteolysis 10-fold by processing

promatrilysin to an active elastolysin via a urokinase-type plasminogen activator-dependent pathway. Matrilysin-deficient human macrophages fail to mediate an elastolytic response despite the continued expression of gelatinase B and **metalloelastase**. Thus, acting in concert with cosecreted cysteine proteinases whose activities are constrained to sites of macrophage-elastin contact (Punturieri, A., S. Filippov, E. Allen, I. Caras, R. Murray, V. Reddy, and S.J. Weiss. 2000. J. Exp. Med. 192:789-799), matrilysin confers macrophages with their most potent MMP-dependent elastolytic system.

CONTROLLED TERM: Animals  
Aorta: CY, cytology  
Aorta: ME, metabolism  
Cathepsins: ME, metabolism  
Cells, Cultured  
Culture Media, Conditioned  
Culture Media, Serum-Free  
\*Elastin: ME, metabolism  
Enzyme Inhibitors: ME, metabolism  
Gelatinase B: ME, metabolism  
Humans  
Macrophages: CY, cytology  
\*Macrophages: ME, metabolism  
Matrilysin: GE, genetics  
\*Matrilysin: ME, metabolism  
Oligonucleotide Array Sequence Analysis  
Pancreatic Elastase: GE, genetics  
Pancreatic Elastase: ME, metabolism  
Plasminogen: ME, metabolism  
Plasminogen Activators: ME, metabolism  
Research Support, U.S. Gov't, P.H.S.  
CAS REGISTRY NO.: 9001-91-6 (Plasminogen); 9007-58-3 (Elastin)  
CHEMICAL NAME: 0 (Culture Media, Conditioned); 0 (Culture Media, Serum-Free); 0 (Enzyme Inhibitors); EC 3.4.- (Cathepsins); EC 3.4.21.- (Plasminogen Activators); EC 3.4.21.36 (Pancreatic Elastase); EC 3.4.24.23 (Matrilysin); EC 3.4.24.35 (Gelatinase B)

L5 ANSWER 8 OF 17 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on  
STN DUPLICATE 2  
ACCESSION NUMBER: 2003:500435 SCISEARCH  
THE GENUINE ARTICLE: 687BG  
TITLE: Ozone-induced disruptions of lung transcriptomes  
AUTHOR: Gohil K (Reprint); Cross C E; Last J A  
CORPORATE SOURCE: Univ Calif Davis, Ctr Comparat Resp & Med, Dept Internal Med, Davis, CA 95616 USA (Reprint)  
COUNTRY OF AUTHOR: USA  
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (6 JUN 2003) Vol. 305, No. 3, pp. 719-728. /  
Publisher: ACADEMIC PRESS INC ELSEVIER SCIENCE, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA.  
ISSN: 0006-291X.  
DOCUMENT TYPE: Article; Journal  
LANGUAGE: English  
REFERENCE COUNT: 60  
ABSTRACT:

We have analyzed changes in similar to 4000 lung mRNAs, with GeneChips, in mice exposed to 1 ppm O<sub>3</sub> for three consecutive nights (8 h per night). Differential gene expression analysis identified similar to 260 O<sub>3</sub> sensitive genes; similar to 80% of these were repressed and similar to 20% were induced in O<sub>3</sub>-exposed mice compared to the air-exposed controls. A 20-fold induction of serum amyloid A3 mRNA by O<sub>3</sub> suggested activation of NF-kappaB and CCAAT/enhancer binding protein-mediated pathways by inflammatory cytokines. Induction (up to 14-fold) of 12 genes that increase DNA synthesis and cell

cycle progression, and increase (similar to 7-fold) in CD44 mRNA and macrophage \*\*\*metalloelastase\*\*\* suggested a state of O<sub>3</sub>-induced hyperplasia and lung remodeling. Several mRNAs encoding enzymes of xenobiotic metabolism and cytoskeletal functions were repressed and may suggest cytokine mediated suppression of cytochrome P450 expression and cachexia-like inflammatory state in ozone-exposed lungs. The expressions of similar to 30 genes of immune response were also repressed. Collectively this genome-wide analysis of lungs identified ozone-induced disruption of gene transcriptional profile indicative of increased cellular proliferation under suppressed immune surveillance and xenobiotic metabolism. (C) 2003 Elsevier Science (USA). All rights reserved.

CATEGORY: BIOCHEMISTRY & MOLECULAR BIOLOGY; BIOPHYSICS  
 SUPPLEMENTARY TERM: cell cycle; transcription factors; cachexia; MHC; immune response; **oligonucleotide** arrays  
 SUPPL. TERM PLUS: NF-KAPPA-B; TUMOR-NECROSIS-FACTOR; CYCLE-DEPENDENT REGULATION; CELL-CYCLE; RIBONUCLEOTIDE REDUCTASE; EPITHELIAL PROLIFERATION; **OLIGONUCLEOTIDE** ARRAYS; GENE-EXPRESSION; END-PRODUCTS; RAT LUNGS

REFERENCE(S):

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
ADACHI N	1997	230	105	BIOCHEM BIOPH RES CO
ARGILES J M	1999	19	223	MED RES REV
BAUD V	2001	11	372	TRENDS CELL BIOL
BING Z Y	2000	275	31616	J BIOL CHEM
CAI L	1999	132	85	TOXICOLOGY
CHANG H R	1998	22	156	JPEN-PARENTER ENTER
CHENG P Y	2001	2	165	CURR DRUG METAB
CHO H Y	2001	280	L537	AM J PHYSIOL-LUNG C
COHEN M D	2001	171	71	TOXICOL APPL PHARM
CRACOWSKI J L	2001	38	93	J VASC RES
DERISI J L	1997	278	680	SCIENCE
DUDEK S M	2001	91	1487	J APPL PHYSIOL
ELLEDGE S J	1990	4	740	GENE DEV
ELSAYED N M	1990	102	1	TOXICOL APPL PHARM
ERIKSSON S	1984	259	11695	J BIOL CHEM
FAKHRZADEH L	2002	26	413	AM J RESP CELL MOL
GELLERT M	2002	71	101	ANNU REV BIOCHEM
GELZLEICHTER T R	1992	112	73	TOXICOL APPL PHARM
GOHIL K	2000	33	831	FREE RADICAL RES
GOLDSTEIN B D	1978		295	CIBA FOUND S
GUTTRIDGE D C	2000	289	2363	SCIENCE
HIROSHIMA K	1987	47	327	EXP MOL PATHOL
HUMPHREYS D	1997	36	15233	BIOCHEMISTRY-US
JAGOE R T	2002	16	1697	FASEB J
JAMALUDDIN M	2001	280	L248	AM J PHYSIOL-LUNG C
JANG A S	2002	57	737	ALLERGY
KAMINSKI N	2000	97	1778	P NATL ACAD SCI USA
KATSUOKA F	1997	238	512	BIOCHEM BIOPH RES CO
KENYON N J	2002	282	L540	AM J PHYSIOL-LUNG C
KLEEGERGER S R	2001	90	713	J APPL PHYSIOL
KOPP E B	1999	11	13	CURR OPIN IMMUNOL
LASKIN D L	2002	234	91	MOL CELL BIOCHEM
LEE E G	2000	289	2350	SCIENCE
LEFFERS H	1993	231	982	J MOL BIOL
LEIKAUF G D	2001			558 RS REP HLTH EFF
LERCHGAGGL A	2002	277	45347	J BIOL CHEM
LI Q T	2002	2	725	NAT REV IMMUNOL
LIEBERAM I	1999	29	2684	EUR J IMMUNOL
LIPSHUTZ R J	1999	21	20	NAT GENET S
LISTON P	1996	379	349	NATURE
LOCKHART D J	1996	14	1675	NAT BIOTECHNOL

LONGPHRE M	1999	86	341	J APPL PHYSIOL
MANGO G W	1998	275	L348	AM J PHYSIOL-LUNG C
NEEPER M	1992	267	14998	J BIOL CHEM
OKITA R T	1996	31	101	CRIT REV BIOCHEM MOL
PRYOR W A	1991	4	341	CHEM RES TOXICOL
PUNJABI C J	1994	11	165	AM J RESP CELL MOL B
RUAN H	2002	51	1319	DIABETES
SCHUSTER J M	2000	67	767	J LEUKOCYTE BIOL
SHASTRI N	2002	20	463	ANNU REV IMMUNOL
SINGAL D P	1996	68	629	INT J CANCER
TIAN B	2002	76	6800	J VIROL
UMBRICHT C B	2001	20	3348	ONCOGENE
VANESS P J	2002	300	824	J PHARMACOL EXP THER
WARD P P	2002	80	95	BIOCHEM CELL BIOL
WATANABE C M H	2001	98	6577	P NATL ACAD SCI USA
WODICKA L	1997	15	1359	NAT BIOTECHNOL
WU L	1991	174	1617	J EXP MED
YARMUSH M L	2002	4	349	ANNU REV BIOMED ENG
ZHAO Q Y	1998	274	L39	AM J PHYSIOL-LUNG C

L5 ANSWER 9 OF 17 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 2003216876 EMBASE  
 TITLE: PTP1B **antisense**-treated mice show regulation of genes involved in lipogenesis in liver and fat.  
 AUTHOR: Waring J.F.; Ciurlionis R.; Clampit J.E.; Morgan S.; Gum R.J.; Jolly R.A.; Kroeger P.; Frost L.; Trevillyan J.; Zinker B.A.; Jirousek M.; Ulrich R.G.; Rondinone C.M.  
 CORPORATE SOURCE: J.F. Waring, Dept. of Cell./Molecular Toxicology, Abbott Laboratories R463, Abbott Park, IL 60064-6104, United States. jeff.waring@abbott.com  
 SOURCE: Molecular and Cellular Endocrinology, (30 May 2003) Vol. 203, No. 1-2, pp. 155-168. ✓  
 Refs: 41  
 ISSN: 0303-7207 CODEN: MCEND6  
 COUNTRY: Ireland  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 003 Endocrinology  
 005 General Pathology and Pathological Anatomy  
 022 Human Genetics  
 030 Pharmacology  
 037 Drug Literature Index  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 20030619  
 Last Updated on STN: 20030619

ABSTRACT: Protein tyrosine phosphatases are important regulators of insulin signal transduction. Our studies have shown that in insulin resistant and diabetic ob/ob and db/db mice, reducing the levels of protein tyrosine phosphatase 1B (PTP1B) protein by treatment with a PTP1B **antisense** \*\*\*oligonucleotide\*\*\* resulted in improved insulin sensitivity and normalized plasma glucose levels. The mechanism by which PTP1B inhibition improves insulin sensitivity is not fully understood. We have used microarray analysis to compare gene expression changes in adipose tissue, liver and muscle of PTP1B \*\*\*antisense\*\*\* -treated ob/ob mice. Our results show that treatment with PTP1B **antisense** resulted in the downregulation of genes involved in lipogenesis in both fat and liver, and a downregulation of genes involved in adipocyte differentiation in fat, suggesting that PTP1B **antisense** acts through a different mechanism than thiazolidinedione (TZD) treatment. In summary, microarray results suggest that reduction of PTP1B may alleviate hyperglycemia and enhance insulin sensitivity by a different mechanism than TZD treatment. .COPYRG. 2003 Elsevier Science Ireland Ltd. All rights reserved.

CONTROLLED TERM:

Medical Descriptors:

- \*lipogenesis
- \*gene expression regulation
- \*diabetes mellitus: ET, etiology
- \*insulin resistance: ET, etiology
- insulin sensitivity
- glucose blood level
- DNA microarray
- adipose tissue
- liver
- muscle tissue
- down regulation
- adipocyte
- cell differentiation
- nucleic acid analysis
- drug effect
- gene control
- histopathology
- nonhuman
- mouse
- animal experiment
- animal model
- controlled study
- animal tissue
- article
- nucleotide sequence
- priority journal

Drug Descriptors:

- \*protein tyrosine phosphatase: EC, endogenous compound
- \*antisense oligonucleotide: CM, drug comparison
- \*antisense oligonucleotide: PD, pharmacology
- \*antisense oligonucleotide: IP, intraperitoneal drug administration
- glucose: EC, endogenous compound
- thiazolidine derivative: CM, drug comparison
- thiazolidine derivative: PD, pharmacology
- thiazolidine derivative: IP, intraperitoneal drug administration
- protein inhibitor: CM, drug comparison
- protein inhibitor: PD, pharmacology
- protein inhibitor: IP, intraperitoneal drug administration
- rosiglitazone: CM, drug comparison
- rosiglitazone: PD, pharmacology
- rosiglitazone: IP, intraperitoneal drug administration
- protein kinase: EC, endogenous compound
- vimentin: EC, endogenous compound
- entactin: EC, endogenous compound
- interferon regulatory factor 7: EC, endogenous compound
- macrophage elastase: EC, endogenous compound
- transcription factor: EC, endogenous compound
- adenylate kinase: EC, endogenous compound
- cytokeratin: EC, endogenous compound
- oncoprotein: EC, endogenous compound
- lymphocyte antigen: EC, endogenous compound
- fructose biphosphatase: EC, endogenous compound
- malate dehydrogenase (decarboxylating): EC, endogenous compound
- adenosine triphosphate citrate lyase: EC, endogenous compound
- cytochrome P450: EC, endogenous compound
- somatomedin: EC, endogenous compound
- oxygase: EC, endogenous compound
- scatter factor: EC, endogenous compound

glucose transporter: EC, endogenous compound  
liver protein: EC, endogenous compound  
membrane protein: EC, endogenous compound  
thyroid hormone receptor: EC, endogenous compound  
cathepsin D: EC, endogenous compound  
CD72 antigen: EC, endogenous compound  
unindexed drug  
isis 113715

CAS REGISTRY NO.: (protein tyrosine phosphatase) 79747-53-8, 97162-86-2;  
(glucose) 50-99-7, 84778-64-3; (rosiglitazone) 122320-73-4,  
155141-29-0; (protein kinase) 9026-43-1; (adenylate kinase)  
9013-02-9; (fructose biphosphatase) 9001-52-9; (malate  
dehydrogenase (decarboxylating)) 9028-46-0, 9074-02-6,  
9080-52-8; (adenosine triphosphate citrate lyase)  
9027-95-6; (cytochrome P450) 9035-51-2; (oxygenase)  
9037-29-0, 9046-59-7; (scatter factor) 67256-21-7,  
72980-71-3; (cathepsin D) 9025-26-7

CHEMICAL NAME: Isis 113715

GENE NUMBER: GENBANK I38444 referred number; GENBANK L32973 referred  
number; GENBANK M11686 referred number; GENBANK M18184  
referred number; GENBANK M33863 referred number; GENBANK  
M55637 referred number; GENBANK M73696 referred number;  
GENBANK M82831 referred number; GENBANK U04827 referred  
number; GENBANK U25844 referred number; GENBANK U41341  
referred number; GENBANK U43084 referred number; GENBANK  
U73037 referred number; GENBANK X14194 referred number;  
GENBANK X51438 referred number; GENBANK X54542 referred  
number; GENBANK X91824 referred number

L5 ANSWER 10 OF 17 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 3

ACCESSION NUMBER: 2003274166 EMBASE

TITLE: Distinct gene expression of osteopontin in patients with  
ulcerative colitis.

AUTHOR: Masuda H.; Takahashi Y.; Asai S.; Takayama T.

CORPORATE SOURCE: Dr. H. Masuda, Third Department of Surgery, Nihon  
University School of Medicine, 2-11-1, Hikarigaoka,  
Nerima-ku, Tokyo 179-0072, Japan. hidekim@med.nihon-u.ac.jp

SOURCE: Journal of Surgical Research, (1 May 2003) Vol. 111, No. 1, /  
pp. 85-90.  
Refs: 35

ISSN: 0022-4804 CODEN: JSGRA2

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 005 General Pathology and Pathological Anatomy  
009 Surgery  
022 Human Genetics  
048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20030724

Last Updated on STN: 20030724

ABSTRACT: Background. Ulcerative colitis (UC) is a multifactorial disorder of  
unknown etiology. Few studies have applied genome-wide gene expression  
analysis in colon tissue samples of UC. We report the analysis of mucosal gene  
expression in UC and noninflamed control specimens. Materials and methods.  
This study included 7 UC patients who received a total colectomy because of  
severe total colitis. Normal control colon tissues were obtained at least 10  
cm from the area of pathology in 3 colon cancer patients. Ten colonic tissue  
samples (7 UC and 3 normal control samples) were subjected to high-density  
\*\*\*oligonucleotide\*\*\* array analysis. To compare differences in the level of  
gene expression between UC and control samples, Mann-Whitney U-test was used,  
with significance set at  $P < 0.05$ . Results. Twenty-five genes had a

3.0.apprx.23.4-fold higher mRNA expression in UC samples compared with normal samples, whereas three genes had a 3.0 .apprx. 3.4-fold lower expression in UC samples compared with normal samples. Two genes showing more than a 10-fold increase expression in UC samples were a macrophage **metalloelastase** (L23808) and a osteopontin (AF052124). It has been said that macrophage **\*\*\*metalloelastase\*\*\*** is related to ulcer formation of the intestine, whereas osteopontin plays an important role in the pathogenesis of systemic lupus erythematosus and rheumatoid arthritis. Conclusion. Our present study supports the previous report that macrophage **metalloelastase** is related to ulcer formation of UC, and it also indicates the possibility that osteopontin plays an important role in the pathogenesis of UC via increased immune activity. .COPYRGHT. 2003 Elsevier Inc. All rights reserved.

CONTROLLED TERM: Medical Descriptors:  
 \*ulcerative colitis: SU, surgery  
 gene expression  
 genetic analysis  
 colon mucosa  
 colon resection  
 disease severity  
 colon  
 colon cancer  
 cancer patient  
 sample  
 DNA microarray  
 rank sum test  
 ulcerogenesis  
 intestine ulcer  
 gene function  
 pathogenesis  
 systemic lupus erythematosus  
 rheumatoid arthritis  
 human  
 clinical article  
 controlled study  
 human tissue  
 adult  
 article  
 nucleotide sequence  
 priority journal  
 Drug Descriptors:  
 \*osteopontin  
 messenger RNA

**macrophage elastase**  
 CAS REGISTRY NO.: (osteopontin) 106441-73-0  
 GENE NUMBER: GENBANK D11139 referred number; GENBANK D87258 referred number; GENBANK J04469 referred number; GENBANK J04599 referred number; GENBANK L06419 referred number; GENBANK L23808 referred number; GENBANK L26232 referred number; GENBANK M14058 referred number; GENBANK M28225 referred number; GENBANK M93221 referred number; GENBANK N74607 referred number; GENBANK U28014 referred number; GENBANK U46573 referred number; GENBANK U77735 referred number; GENBANK X15334 referred number; GENBANK X81832 referred number; GENBANK X92997 referred number; GENBANK Y14690 referred number; GENBANK AA100961 referred number; GENBANK AF004230 referred number; GENBANK AF022797 referred number; GENBANK AF052124 referred number; GENBANK AF055376 referred number; GENBANK AJ000342 referred number; GENBANK AL049946 referred number; GENBANK AY029208 referred number

L5 ANSWER 11 OF 17 MEDLINE on STN  
 ACCESSION NUMBER: 2002347958 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12091409  
TITLE: Microarray analysis of corneal fibroblast gene expression after interleukin-1 treatment.  
AUTHOR: Mahajan Vinit B; Wei Cui; McDonnell Peter J 3rd  
CORPORATE SOURCE: Department of Microbiology and Molecular Genetics, University of California-Irvine, Irvine, CA 92697, USA.  
SOURCE: Investigative ophthalmology & visual science, (2002 Jul) 43 (7) 2143-51. X  
Journal code: 7703701. ISSN: 0146-0404.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200207  
ENTRY DATE: Entered STN: 20020702  
Last Updated on STN: 20020716  
Entered Medline: 20020715

ABSTRACT:

PURPOSE: To identify changes in gene expression in human corneal fibroblasts after exposure to interleukin-1 $\alpha$ . METHODS: RNA was isolated from cultured human corneal fibroblasts after treatment with interleukin-1 $\alpha$  and subjected to DNA microarray analysis. Changes in gene expression were determined by comparison with untreated cells in three independent experiments after a Bayesian statistical analysis of variance. RESULTS: Changes in gene expression were reproducibly observed in 165 genes representing previously identified and novel chemokines, matrix molecules, membrane receptors, angiogenic mediators, and transcription factors that correlated with pathophysiological responses to inflammation. Dramatic increases in gene expression were observed with exodus-1 (CCL20), MMP-12, and RhoA. CONCLUSIONS: DNA microarray analysis of the corneal fibroblast response to interleukin-1 $\alpha$  provides important insight into modeling changes in gene expression and suggests novel therapeutic targets for the control of corneal inflammation.

CONTROLLED TERM: Cells, Cultured  
Computational Biology: MT, methods  
\*Cornea: DE, drug effects  
Cornea: ME, metabolism  
\*Eye Proteins: GE, genetics  
Eye Proteins: ME, metabolism  
\*Fibroblasts: DE, drug effects  
Fibroblasts: ME, metabolism  
\*Gene Expression: PH, physiology  
Gene Expression Profiling  
Humans  
\*Interleukin-1: PD, pharmacology  
**Oligonucleotide Array Sequence Analysis**  
RNA: IP, isolation & purification  
Research Support, Non-U.S. Gov't

CAS REGISTRY NO.: 63231-63-0 (RNA)  
CHEMICAL NAME: 0 (Eye Proteins); 0 (Interleukin-1)

L5 ANSWER 12 OF 17 MEDLINE on STN

ACCESSION NUMBER: 2002499097 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12235077  
TITLE: Upregulation of matrix metalloproteinases in a model of T cell mediated tissue injury in the gut: analysis by gene array and in situ hybridisation.  
AUTHOR: Salmela M T; MacDonald T T; Black D; Irvine B; Zhuma T; Saarialho-Kere U; Pender S L F  
CORPORATE SOURCE: Department of Dermatology, Helsinki University Central Hospital, Helsinki, Finland.  
SOURCE: Gut, (2002 Oct) 51 (4) 540-7.  
Journal code: 2985108R. ISSN: 0017-5749.  
PUB. COUNTRY: England: United Kingdom



DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 200211  
ENTRY DATE: Entered STN: 20021004  
Last Updated on STN: 20021213  
Entered Medline: 20021107

ABSTRACT:

BACKGROUND AND AIM: Matrix metalloproteinases (MMPs) have been implicated in tissue remodelling and ulceration in inflammatory bowel disease and coeliac disease. Studies to date have concluded that stromelysin 1 is functionally involved in mucosal degradation. However, there are many other MMPs whose function in the gut is currently unknown. This work had two aims: firstly, to use gene array technology to measure changes in MMP and tissue inhibitor of metalloproteinase (TIMP) expression in a model of T cell mediated injury in the gut, and secondly, to correlate data from gene arrays with that generated by in situ hybridisation. METHODS: T cells in explants of human fetal gut were activated with pokeweed mitogen or anti-CD3 plus interleukin 12. Gene array analysis and in situ hybridisation were performed to investigate changes in MMP gene expression. RESULTS: Both gene array analysis and in situ hybridisation indicated marked upregulation of stromelysin 2 and macrophage \*\*\*metalloelastase\*\*\* expression in the explants associated with mucosal destruction. The arrays also confirmed our previous observation that interstitial collagenase (MMP-1), stromelysin 1 (MMP-3), and gelatinase B (MMP-9) are upregulated but there was no change in MMP-2, -7, -8, -9, -11, -13, -14-17, or -19. Following T cell activation, transcripts for TIMPs were reduced. CONCLUSIONS: These results show that there is differential upregulation of MMPs during T cell responses in the gut and suggest that further studies on the role of stromelysin 2 and macrophage \*\*\*metalloelastase\*\*\* may show that they have a functional role. In addition, the increase in MMPs and reduction in TIMPs suggest that the protease/antiprotease balance in the mucosa may determine the extent of mucosal degradation.

CONTROLLED TERM: Collagenases: GE, genetics  
Humans  
In Situ Hybridization  
\*Intestine, Small: EN, enzymology  
Matrilysin: GE, genetics  
Matrilysin: ME, metabolism  
Matrix Metalloproteinases: GE, genetics  
\*Matrix Metalloproteinases: ME, metabolism  
Metalloendopeptidases: GE, genetics  
Metalloendopeptidases: ME, metabolism  
**Oligonucleotide Array Sequence Analysis**  
RNA: AN, analysis  
Research Support, Non-U.S. Gov't  
\*T-Lymphocytes: IM, immunology  
Tissue Inhibitor of Metalloproteinase-1: GE, genetics  
Tissue Inhibitor of Metalloproteinase-3: IM, immunology  
Tissue Inhibitor of Metalloproteinases: GE, genetics  
\*Tissue Inhibitor of Metalloproteinases: ME, metabolism  
\*Up-Regulation  
CAS REGISTRY NO.: 63231-63-0 (RNA)  
CHEMICAL NAME: 0 (Tissue Inhibitor of Metalloproteinase-1); 0 (Tissue Inhibitor of Metalloproteinase-3); 0 (Tissue Inhibitor of Metalloproteinases); EC 3.4.24 (Metalloendopeptidases); EC 3.4.24.- (Collagenases); EC 3.4.24.- (Matrix Metalloproteinases); EC 3.4.24.- (alveolar macrophage elastase); EC 3.4.24.- (collagenase 3); EC 3.4.24.- (membrane-type matrix metalloproteinase); EC 3.4.24.22 (stromelysin 2); EC 3.4.24.23 (Matrilysin)

L5 ANSWER 13 OF 17 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 2002209396 EMBASE  
TITLE: Matrix metalloproteinases: Promoters of tumor progression  
and invasiveness.  
AUTHOR: Sela B.-A.  
CORPORATE SOURCE: Dr. B.-A. Sela, Institute of Chemical Pathology, Sheba  
Medical Center, Tel Hashomer 52621, Israel.  
benamis@sheba.health.gov.il  
SOURCE: Israel Medical Association Journal, (2002) Vol. 4, No. 4, ✓  
pp. 280-282.  
Refs: 30  
ISSN: 1565-1088 CODEN: IMAJCX  
COUNTRY: Israel  
DOCUMENT TYPE: Journal; Editorial  
FILE SEGMENT: 016 Cancer  
037 Drug Literature Index  
030 Pharmacology  
029 Clinical Biochemistry  
LANGUAGE: English  
ENTRY DATE: Entered STN: 20020708  
Last Updated on STN: 20020708  
CONTROLLED TERM: Medical Descriptors:  
\*cancer growth  
\*cancer invasion  
human  
clinical trial  
nonhuman  
metastasis  
angiogenesis  
protein degradation  
in vivo study  
enzyme activity  
breast cancer: DT, drug therapy  
colorectal cancer: DT, drug therapy  
prostate cancer: DT, drug therapy  
skin cancer  
ovary cancer  
bladder cancer  
thyroid cancer: DI, diagnosis  
thyroid papillary carcinoma: DI, diagnosis  
enzyme activation  
protein expression  
cancer diagnosis  
cancer cell  
enzyme inhibition  
drug mechanism  
phage display  
adenovirus vector  
editorial  
Drug Descriptors:  
\*matrix metalloproteinase: EC, endogenous compound  
tumor promoter: EC, endogenous compound  
tissue inhibitor of metalloproteinase: EC, endogenous  
compound  
gelatinase A: EC, endogenous compound  
matrilysin: EC, endogenous compound  
gelatinase B: EC, endogenous compound  
proteoglycan: EC, endogenous compound  
tissue inhibitor of metalloproteinase 2: EC, endogenous  
compound  
messenger RNA: EC, endogenous compound  
tissue inhibitor of metalloproteinase 1: EC, endogenous

compound

**macrophage elastase: EC, endogenous compound**

angiostatin: EC, endogenous compound

matrix metalloproteinase inhibitor: CT, clinical trial

matrix metalloproteinase inhibitor: PD, pharmacology

matrix metalloproteinase inhibitor: DT, drug therapy

bb 3103: CT, clinical trial

bb 3103: PD, pharmacology

chelating agent: CT, clinical trial

chelating agent: PD, pharmacology

pyrimidine 2,4,6 trione: PD, pharmacology

decapeptide: PD, pharmacology

**antisense oligonucleotide: PD, pharmacology**

furin: EC, endogenous compound

stromelysin 3: EC, endogenous compound

stromelysin: EC, endogenous compound

interleukin 1beta: EC, endogenous compound

trypsin inhibitor: PD, pharmacology

unclassified drug

CAS REGISTRY NO.: (tissue inhibitor of metalloproteinase) 97837-28-0;  
(gelatinase A) 146480-35-5; (matrilysin) 141256-52-2;  
(gelatinase B) 146480-36-6; (tissue inhibitor of  
metalloproteinase 2) 124861-55-8; (tissue inhibitor of  
metalloproteinase 1) 140208-24-8; (angiostatin)  
172642-30-7, 86090-08-6; (stromelysin 3) 145267-01-2;  
(stromelysin) 79955-99-0; (trypsin inhibitor) 9035-81-8  
CHEMICAL NAME: Bb 3103  
COMPANY NAME: Hoffmann La Roche

L5 ANSWER 14 OF 17 MEDLINE on STN  
ACCESSION NUMBER: 2002161865 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11893658  
TITLE: Roger S. Mitchell lecture. Uses of expression microarrays  
in studies of pulmonary fibrosis, asthma, acute lung  
injury, and emphysema.  
AUTHOR: Sheppard Dean  
CORPORATE SOURCE: Lung Biology Center, Center for Occupational and  
Environmental Health, Cardiovascular Research Institute,  
Department of Medicine, University of California, San  
Francisco, San Francisco, CA 94143, USA..  
deans@itsa.ucsf.edu  
SOURCE: Chest, (2002 Mar) 121 (3 Suppl) 21S-25S.  
Journal code: 0231335. ISSN: 0012-3692.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: (LECTURES)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 200204  
ENTRY DATE: Entered STN: 20020315  
Last Updated on STN: 20020418  
Entered Medline: 20020417

**ABSTRACT:**

Expression microarrays are a powerful tool that could provide new information about the molecular pathways regulating common lung diseases. To exemplify how this tool can be useful, selected examples of informative experiments are reviewed. In studies relevant to asthma, the cytokine interleukin-13 has been shown to produce many of the phenotypic features of this disease, but the cellular targets in the airways and the molecular pathways activated are largely unknown. We have used microarrays to begin to dissect the different transcriptional responses of primary lung cells to this cytokine. In experiments designed to identify global transcriptional programs responsible for regulating lung inflammation and pulmonary fibrosis, we performed microarray experiments on lung tissue from wild-type mice and mice lacking a

member of the integrin family known to be involved in activation of latent transforming growth factor (TGF)-beta. In addition to identifying distinct clusters of genes involved in each of these processes, these studies led to the identification of novel pathways by which TGF-beta can regulate acute lung injury and emphysema. Together, these examples demonstrate how careful application and thorough analysis of expression microarrays can facilitate the discovery of novel molecular targets for intervening in common lung diseases.

CONTROLLED TERM: Check Tags: In Vitro  
Animals  
\*Antigens, Neoplasm  
\*Asthma: GE, genetics  
Gene Expression  
\*Genes, Regulator  
Genetic Predisposition to Disease  
Humans  
Integrins: GE, genetics  
Interleukin-13: PH, physiology  
Lung: CY, cytology  
Lung: ME, metabolism  
Lung: PA, pathology  
Matrilysin: GE, genetics  
Metalloendopeptidases: GE, genetics  
Mice  
Mice, Knockout

**\*Oligonucleotide Array Sequence Analysis**

\*Pulmonary Emphysema: GE, genetics  
\*Pulmonary Fibrosis: GE, genetics  
Pulmonary Fibrosis: PA, pathology  
\*Respiratory Distress Syndrome, Adult: GE, genetics  
Trans-Activation (Genetics)  
Transforming Growth Factor beta: GE, genetics  
CHEMICAL NAME: 0 (Antigens, Neoplasm); 0 (Integrins); 0 (Interleukin-13);  
0 (Transforming Growth Factor beta); 0 (integrin  
alpha v beta 6); EC 3.4.24 (Metalloendopeptidases); EC  
3.4.24.- (alveolar **macrophage elastase**  
); EC 3.4.24.23 (Matrilysin)

L5 ANSWER 15 OF 17 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 2001261021 EMBASE  
TITLE: [Analysis of gene expression with microarrays - Application  
in medicine].  
BADANIE EKSPRESJI GENOW METODA MICROARRAY - PERSPEKTYWY  
WYKORZYSTANIA W MEDYCYNIE.  
AUTHOR: Pawliczak R.; Kowalski M.L.  
CORPORATE SOURCE: R. Pawliczak, Kat. Zaklad Immunol. Klin. AM Lodzi, ul.  
Pomorska 251, 92-213 Lodz, Poland  
SOURCE: Alergia Astma Immunologia, (2001) Vol. 6, No. 2, pp. 77-85.  
Refs: 28  
ISSN: 1427-3101 CODEN: AAIMFF  
COUNTRY: Poland  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 022 Human Genetics  
027 Biophysics, Bioengineering and Medical  
Instrumentation  
LANGUAGE: Polish  
SUMMARY LANGUAGE: English; Polish  
ENTRY DATE: Entered STN: 20010815  
Last Updated on STN: 20010815

ABSTRACT: Microarrays are one of the latest breakthroughs in experimental molecular biology, which allow monitoring of gene expression for tens of thousands of genes in parallel and are already producing huge amounts of valuable data. Microarray RNA expression on a genome-wide scale is now a

proven technology, although the idea of analysis of expression many genes in one sample is not new. The development of clone printing technology and \*\*\*oligonucleotide\*\*\* synthesis allowed to produce high-density microarray. These systems together with more powerful and fast computer and software systems were applied not only in basic science but also in clinical medicine and pharmaceutical industry. In this publication the authors provide the information about the technology, available detection systems and data analysis software. Comprehensive review of current and fundamental papers using microarray technology application in rheumatoid arthritis, oncology, cystic fibrosis research, and allergic airways inflammation is also included.

CONTROLLED TERM: Medical Descriptors:  
\*DNA microarray  
gene expression  
analytic method  
molecular cloning  
nucleotide metabolism  
computer system  
computer program  
clinical medicine  
drug industry  
data analysis  
reverse transcription polymerase chain reaction  
review  
Drug Descriptors:  
complementary RNA  
gelatinase A  
granulocyte colony stimulating factor  
macrophage elastase  
oligonucleotide  
STAT protein  
stromelysin  
tissue inhibitor of metalloproteinase  
CAS REGISTRY NO.: (gelatinase A) 146480-35-5; (stromelysin) 79955-99-0;  
(tissue inhibitor of metalloproteinase) 97837-28-0

L5 ANSWER 16 OF 17 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 4

ACCESSION NUMBER: 1998095538 EMBASE  
TITLE: Overview of matrix metalloproteinase expression in cultured human cells.  
AUTHOR: Giambernardi T.A.; Grant G.M.; Taylor G.P.; Hay R.J.; Maher V.M.; McCormick J.J.; Klebe R.J.  
CORPORATE SOURCE: T.A. Giambernardi, Dept Cellular and Structural Biology, Univ of Texas Health Science Center, San Antonio, TX, United States  
SOURCE: Matrix Biology, (1998) Vol. 16, No. 8, pp. 483-496.  
Refs: 88  
ISSN: 0945-053X CODEN: MTBOEC  
COUNTRY: Germany  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 016 Cancer  
021 Developmental Biology and Teratology  
029 Clinical Biochemistry  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 19980409  
Last Updated on STN: 19980409

ABSTRACT: The matrix metalloproteinases (MMP) have been implicated in tumor invasion and metastasis both by immunohistochemical studies and from the observation that specific metalloproteinase inhibitors block tumor invasion and metastasis. **Oligonucleotide** primers for thirteen MMPs (MMP-1, MMP-2, MMP-3, MMP-7, MMP-8, MMP-9, MMP-10, MMP-11, **MMP-12**, MMP-13,

MMP-14, MMP-15, MMP-16) were optimized for use in RT-PCR. A semi-quantitative RT-PCR assay was used to determine the pattern of MMP mRNA expression in 84 normal and transformed or carcinogen transformed human cell lines and strains derived from different tissues. The results demonstrate one or more cell lines which express thirteen members of the MMP family. In addition, various oncogene transfected human fibroblast cell strains were analyzed for MMP expression. We confirm that over-expression of the H-ras oncoprotein correlates with up-regulation of MMP-9 and demonstrate that over-expression of v-sis also up-regulates MMP-9. A cell line immortalized following myc expression was found to up-regulate MMP-7, MMP-11 and MMP-13. Inappropriate expression of several MMP mRNAs was detected in breast, prostate, bone, colon and oral tumor derived cell lines. Identification of at least one cell line expressing each of thirteen MMPs and the observation of oncogene induced expression of several MMPs should facilitate analysis of the transcriptional mechanisms controlling each MMP.

CONTROLLED TERM: Medical Descriptors:  
protein expression  
oligonucleotide probe  
reverse transcription polymerase chain reaction  
cell transformation  
oncogene  
genetic transfection  
fibroblast  
gene overexpression  
oncogene h ras  
cell immortalization  
tumor cell: ET, etiology  
breast tumor: ET, etiology  
prostate tumor: ET, etiology  
bone tumor: ET, etiology  
colon tumor: ET, etiology  
mouth tumor: ET, etiology  
human  
controlled study  
human cell  
article  
priority journal  
Drug Descriptors:  
\*matrix metalloproteinase: EC, endogenous compound  
messenger rna: EC, endogenous compound  
carcinogen  
collagenase: EC, endogenous compound  
gelatinase a: EC, endogenous compound  
stromelysin: EC, endogenous compound  
matrilysin: EC, endogenous compound  
neutrophil collagenase: EC, endogenous compound  
gelatinase b: EC, endogenous compound  
stromelysin 2: EC, endogenous compound  
CAS REGISTRY NO.: (collagenase) 9001-12-1; (gelatinase a) 146480-35-5;  
(stromelysin) 79955-99-0; (matrilysin) 141256-52-2;  
(gelatinase b) 146480-36-6

L5 ANSWER 17 OF 17 MEDLINE on STN  
ACCESSION NUMBER: 96275569 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 8686751  
TITLE: Expression of most matrix metalloproteinase family members  
in breast cancer represents a tumor-induced host response.  
AUTHOR: Heppner K J; Matrisian L M; Jensen R A; Rodgers W H  
CORPORATE SOURCE: Department of Cell Biology, Vanderbilt University,  
Nashville, Tennessee, USA.  
CONTRACT NUMBER: R01 CA50468 (NCI)  
R01 HD30472 (NICHD)

RO3 CA54942 (NCI)

+

SOURCE: American journal of pathology, (1996 Jul) 149 (1) 273-82.  
Journal code: 0370502. ISSN: 0002-9440.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 199608  
ENTRY DATE: Entered STN: 19960828  
Last Updated on STN: 20000303  
Entered Medline: 19960821

ABSTRACT:

Matrix metalloproteinase (MMP) family members have been associated with advanced-stage cancer and contribute to tumor progression, invasion, and metastasis as determined by inhibitor studies. In situ hybridization was performed to analyze the expression and localization of all known MMPs in a series of human breast cancer biopsy specimens. Most MMPs were localized to tumor stroma, and all MMPs had very distinct expression patterns. Matrilysin was expressed by morphologically normal epithelial ducts within tumors and in tissue from reduction mammoplasties, and by epithelial-derived tumor cells. Many family members, including stromelysin-3, gelatinase A, MT-MMP, interstitial collagenase, and stromelysin-1 were localized to fibroblasts of tumor stroma of invasive cancers but in quite distinct, and generally widespread, patterns. Gelatinase B, collagenase-3, and **metalloelastase** expression were more focal; gelatinase B was primarily localized to endothelial cells, collagenase-3 to isolated tumor cells, and **metalloelastase** to cytokeratin-negative, macrophage-like cells. The MMP inhibitor, TIMP-1, was expressed in both stromal and tumor components in most tumors, and neither stromelysin-2 nor neutrophil collagenase were detected in any of the tumors. These results indicate that there is very tight and complex regulation in the expression of MMP family members in breast cancer that generally represents a host response to the tumor and emphasize the need to further evaluate differential functions for MMP family members in breast tumor progression.

CONTROLLED TERM: Check Tags: Female

**Antisense Elements (Genetics)**

\*Breast Neoplasms: CH, chemistry  
Breast Neoplasms: PP, physiopathology  
Carcinoma in Situ: CH, chemistry  
Carcinoma in Situ: PP, physiopathology  
Carcinoma, Ductal, Breast: CH, chemistry  
Carcinoma, Ductal, Breast: PP, physiopathology  
Endothelium: CH, chemistry  
Epithelium: CH, chemistry  
Fibroblasts: CH, chemistry  
Humans  
In Situ Hybridization  
\*Metalloendopeptidases: AN, analysis  
Metalloendopeptidases: GE, genetics  
RNA, Messenger: AN, analysis  
Research Support, U.S. Gov't, Non-P.H.S.  
Research Support, U.S. Gov't, P.H.S.

CHEMICAL NAME: 0 (**Antisense Elements (Genetics)**); 0 (RNA, Messenger); EC 3.4.24 (Metalloendopeptidases)

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